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Title Pharmacokinetic advantage of intraperitoneal injection of docetaxel in the treatment of dissemination of cancer in mice

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Abstract Intraperitoneal administration of docetaxel has been used to treat peritoneal dissemination of cancer, but its safety has not been confirmed. We have compared the pharmacokinetic behaviour of docetaxel after intravenous and intraperitoneal administration in nu/nu mice bearing MKN45P, a gastric cancer variant line producing peritoneal dissemination. Docetaxel (8 mg kg⁻¹) was intraperitoneally injected into the mice and at designated times the drug concentration was measured in plasma, and abdominal tissues (liver, kidney, intestine and spleen, solid cancer, and suspended free cancer). The pharmacokinetics of docetaxel was similar in control mice and cancer-bearing mice after administration via either route, except that the transfer of docetaxel from the abdominal cavity to systemic blood (plasma) was slower in cancer-bearing mice than in control mice. As expected, intraperitoneal drug concentration was much higher (approximately 100-fold) and was maintained for a longer time in the intraperitoneal injection group than in the intravenous injection group. The drug concentrations in peritoneal solid cancer tissue and cancer cells were also significantly higher for a longer time in the intraperitoneal injection group than in the intravenous injection group. The values of the plasma area under concentration-time curves (AUC) were similar for both administration routes. The AUC of docetaxel in ascite/AUC plasma after intraperitoneal administration was higher than after intravenous administration. The drug concentration in abdominal organs after intraperitoneal injection was lower during the first 2 h, then became similar to those after intravenous injection. These results indicated that the intraperitoneal administration of docetaxel for peritoneal dissemination was likely to be a better treatment method, without causing any increase in systemic toxicity.

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